Probing the Glycopolymer-Ion Interaction *via* Specific Ion Effects

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Experimental Section

Materials

Di(ethylene glycol) ethyl ether acrylate (DEGEEA, ≥ 90%, Aladdin) and poly(ethylene glycol) methyl ether acrylate ($PEGA_{480}$, average M_n 480, Aladdin) were purified by passing the monomer through a column filled with neutral alumina to remove the inhibitor. Glycidyl acrylate (GA), 1-(2'-propargyl) D-ribose and tris(2-(dimethylamino)ethyl)amine (Me_6TREN) were synthesized according to a literature procedure and stored in a freezer under nitrogen atmosphere.[1-5] Ethyl α-bromoisobutyrate (EBiB, 99%, Aladdin), *N, N*-dimethylbenzamide (DMF, 99%, Aladdin), Dimethyl sulfoxide (DMSO, 99%, Aladdin), 2, 2'-bipyridyl (bpy, 99%, Aladdin), sodium azide (99%, Aladdin) were used as received. Membrane dialysis (1 K MWCO) was obtained from Spectrum Laboratories. All other reagents and solvents were obtained from Aladdin (China) and used without further purification unless otherwise stated.

Instruments and analysis

^1H NMR spectra were recorded at 25 °C with a Bruker AV 500 M spectrometer using deuterated solvents obtained from Aladdin. The number-average molecular weight (M_n) and the molecular weight distribution (M_w/M_n) were determined by Waters 1515 size exclusion chromatography (SEC) in N,N-dimethylbenzamide (DMF) at 40 °C with a flow rate of 1.00 mL min^{-1}. The SEC was equipped with refractive index (RI) and UV detectors, a 20 μm guard column (4.6 mm × 30 mm, 100–10 K) followed by three Waters Styragel columns (HR1, HR3 & HR4) and an autosampler. Narrow linear polystyrene standards in the range of 540 to 7.4×10^5 g mol^{-1} were used to calibrate the system. All samples were passed through a 0.45 μm PTFE filter before analysis. Fourier transform infrared (FTIR) spectra were recorded on a Nicolet iS5 FTIR spectrometer using an iD7 diamond attenuated total reflectance optical base. Thermal gravimetric analysis (TGA, Mettler Toledo, Switzerland) was performed at a heating rate of 10 °C min^{-1} from 50 ℃ to 700 ℃ under nitrogen protection. The size and size distribution of the glycopolymers in the presence of 1, 4-phenylenebisboronic acid were measured by dynamic light scattering (DLS) using a ZetaPALS variable temperature analyzer (Brookhaven Instruments, UK). The optical transmittance of the aqueous solution of thermoresponsive polymers at a wavelength of 500 nm was acquired on a SHIMADZU UV-2600 UV/Vis spectrophotometer. A thermostatically controlled cuvette was employed and the heating rate was 1 ℃ min^{-1}. The cloud point was defined as the temperature where the absorbance increased to 50% in the second heating run.

Synthesis of thermoresponsive nonlinear PEG analogues *via* Cu(0)-RDRP

The Cu(0)-RDRP was performed using the standard Schlenk technique under nitrogen protection. To a Schlenk tube fitted with a rubber stopper, EBiB (59 μL, 0.4 mmol), Me_6TREN (19 μL, 0.072 mmol), $CuBr_2$ (8.9 mg, 0.04 mmol), DEGEEA (7520 mg, 40 mmol), $PEGA_{480}$ (2304 mg, 4.8 mmol) and DMSO (5 mL) were charged and the mixture was bubbled with nitrogen for 15 min. The copper wire (5 cm) was wound around a magnetic stir bar and washed sequentially with acetic acid, ethanol and then dried nitrogen. After that, the copper wire was transferred to the first Schlenk tube. The Schlenk tube was sealed and the light green solution was allowed to polymerize at 25 ℃. After 12 h, the reaction was stopped *via* exposure to the air and the mixture was diluted with water and dialyzed against water for 48 h. Finally, the random copolymer (poly(DEGEEA)-*r*-(PEGA$_{480}$), 9326 mg, 95%) could be recovered *via* lyophilization.

Synthesis of epoxy-containing random copolymer poly(DEGEEA)-r-(GA) *via* Cu(0)-RDRP

To a Schlenk tube fitted with a rubber stopper, EBiB (59 µL, 0.4 mmol), Me$_6$TREN (19 µL, 0.072 mmol), CuBr$_2$ (8.9 mg, 0.04 mmol), DEGEEA (6016 mg, 32 mmol), GA (521 mg, 4 mmol) and DMSO (5 mL) were charged and the mixture was bubbled with nitrogen for 15 min. The copper wire (5 cm) was wound around a magnetic stir bar and washed sequentially with acetic acid, ethanol and then dried nitrogen. After that, the copper wire was transferred to the first Schlenk tube. The Schlenk tube was sealed and the light green solution was allowed to polymerize at 25 °C. After 12 h, the reaction was stopped *via* exposure to the air and the mixture was diluted with water and dialyzed against water for 48 h. Finally, the random copolymer (poly(DEGEEA)-*r*-(GA), 5845 mg, 90%) could be recovered *via* lyophilization.

Synthesis of thermoresponsive glycopolymer *via* click reaction

Epoxy-containing polymer (poly(DEGEEA)-*r*-(GA), 500 mg, containing 0.31 mmol epoxide groups) was dissolved in DMF (5 mL). Sodium azide (30 mg, 0.47 mmol) and ammonium chloride (24.7 mg, 0.47 mmol) were added to the solution and stirred at 50 °C for 24 h. After cooling down to ambient temperature, the mixture was directly transferred to a dialysis tubing and dialyzed against water for two days. 471.32 mg (88.9%) Azide-functionalized polymer (poly(DEGEEA)-*r*-(Azide), 472 mg, 89%) was obtained after drying under vacuum at ambient temperature.

Subsequently, the solution of azide-containing copolymer (poly(DEGEEA)-*r*-(Azide), 400 mg, containing ~0.24 mmol azide groups), 1-(2'-propargyl) D-ribose (72 mg, 0.48 mmol), bpy (7.8 mg, 0.05 mmol) in DMF (5 mL) was deoxygenated by three freeze-pump-thaw cycles. The solution was then transferred *via* cannula under nitrogen into a Schlenk tube, previously evacuated and filled with nitrogen, containing CuBr (10 mg, 0.07 mmol). The resulting brown solution was stirred at 25 ℃ for 24 h. When the reaction was completed, the reaction mixture was diluted with water (20 mL) and purged with air for 1 h and then dialyzed against water for two days. Finally, thermoresponsive glycopolymer (poly(DEGEEA)-*r*-(Ribose), 416 mg, 95%) was recovered after lyophilization.

Synthesis of poly(GA) *via* Cu(0)-RDRP

To a Schlenk tube fitted with a rubber stopper, EBiB (59 μL, 0.4 mmol), Me_6TREN (19 μL, 0.072 mmol), $CuBr_2$ (8.9 mg, 0.04 mmol), GA (1024 mg, 8 mmol) and DMSO (5 mL) were charged and the mixture was bubbled with nitrogen for 15 min. The copper wire (5 cm) was wound around a magnetic stir bar and washed sequentially with acetic acid, ethanol and then dried nitrogen. After that, the copper wire was transferred to the first Schlenk tube. The Schlenk tube was sealed and the light green solution was allowed to polymerize at 25 ℃. After 12 h, the reaction was stopped *via* exposure to the air and the mixture was diluted with water and dialyzed against water for 48 h. Finally, the homopolymer (poly(GA), 915 mg, 89%) could be recovered *via* lyophilization.

Synthesis of poly(Ribose) *via* click reaction

Poly(GA) (200 mg, containing 1.56 mmol epoxide groups) was dissolved in DMF (5 mL). Sodium azide (152 mg, 2.34 mmol) and ammonium chloride (125 mg, 2.34 mmol) were added to the solution and stirred at 50 °C for 24 h. After cooling down to ambient temperature, the mixture was directly transferred to dialysis tubing and dialyzed against water for two days. Finally, the homopolymer (poly(Azide), 275 mg, 91%) could be recovered *via* lyophilization.

Subsequently, the solution of azide-containing homopolymer (poly(Azide), 200 mg, containing ~1.33 mmol azide groups), 1-(2'-propargyl) D-ribose (400 mg, 2.67 mmol), bpy (42 mg, 0.27 mmol) in DMF (5 mL) was deoxygenated by three freeze-pump-thaw cycles. The solution was then transferred *via* cannula under nitrogen into a Schlenk tube, previously evacuated and filled with nitrogen, containing CuBr (10 mg, 0.07 mmol). The resulting brown solution was stirred at 25 °C for 24 h. When the reaction was completed, the reaction mixture was diluted with water (20 mL) and purged with air for 1 h and then dialyzed against water for two days. Finally, glycopolymer (poly(Ribose), 384 mg, 96%) was recovered after lyophilization.

Interactions of polymers with boric acid, $(CH_3COO)_2Pb$ and Na_2HAsO_4

Poly(DEGEEA)-*r*-($PEGA_{480}$) or poly(Ribose) (12.5 mg/mL) was solubilized in the aqueous solution containing boric acid (200 mM) or $(CH_3COO)_2Pb$ (110 mM) or Na_2HAsO_4 (125 mM) and stirred for 12 hours. Subsequently, the solution was dialyzed (MWCO: 1000 Da) against excess water for 2 days to remove the salts. The polymers were then recovered *via* lyophilization.

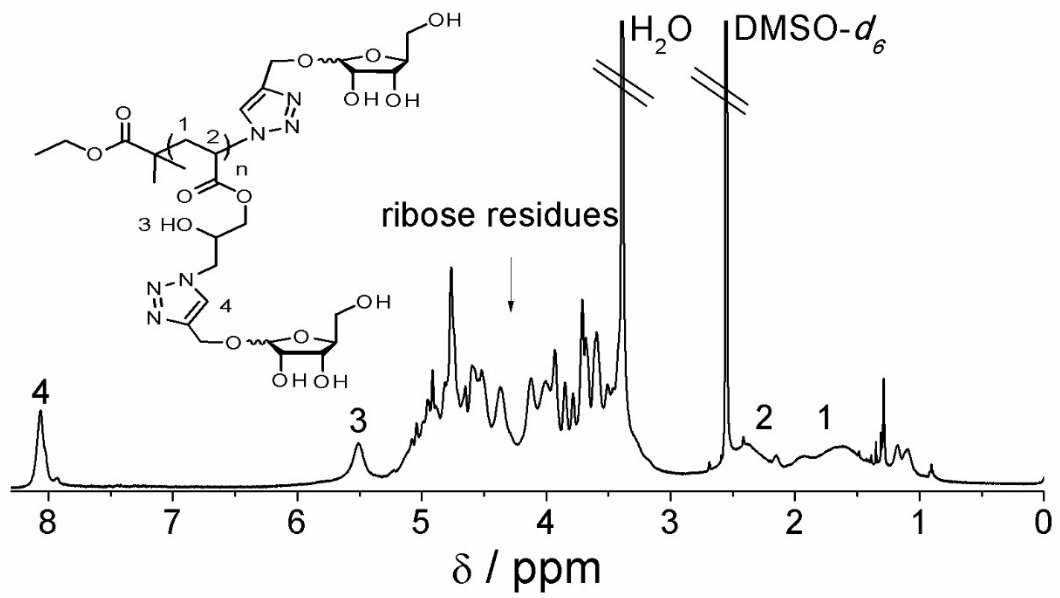

Figure S1. ^{1}H NMR spectrum of poly(Ribose) in DMSO-d_6.

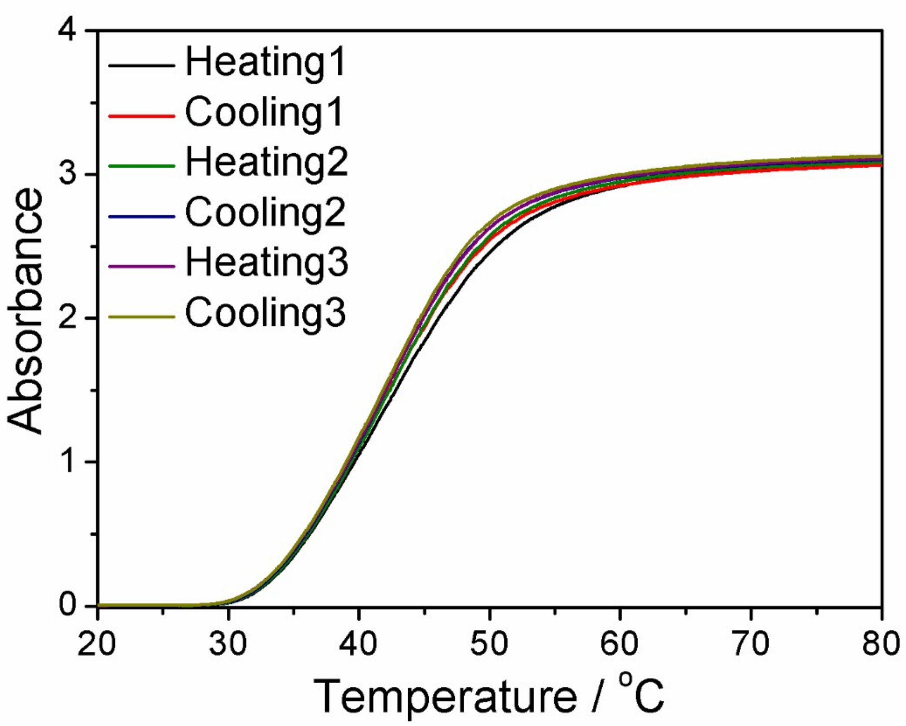

Figure S2. Temperature dependence of the absorbance at 500 nm obtained for 2 mg mL^{-1} aqueous solutions of poly(DEGEEA)-*r*-(Ribose). A thermostatically controlled cuvette was employed and the heating rate was 1 °C min^{-1}.

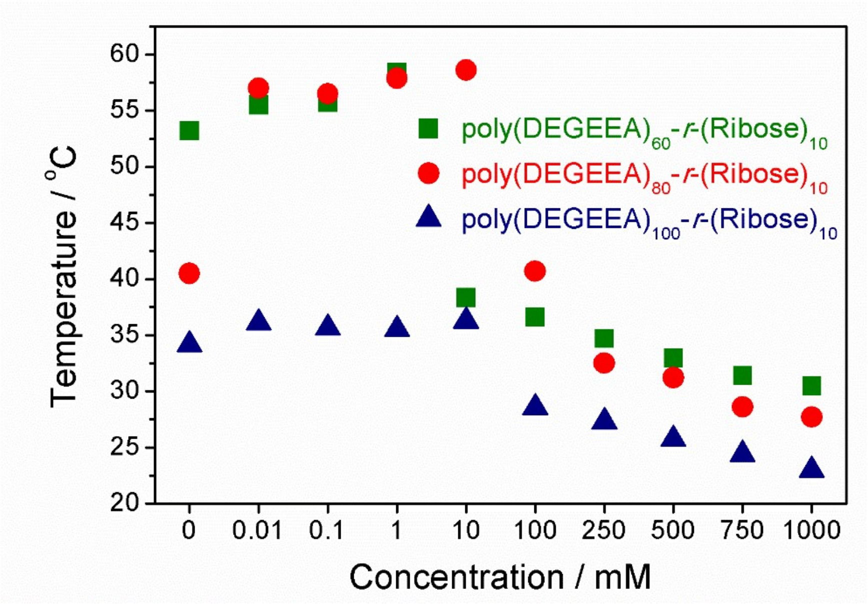

Figure S3. The effect of different contents of ribose on the cloud point of glycopolymers in the aqueous solution of NaCl (0-1000 mM). The concentrations of polymers in the solution are all 2 mg mL^{-1}.

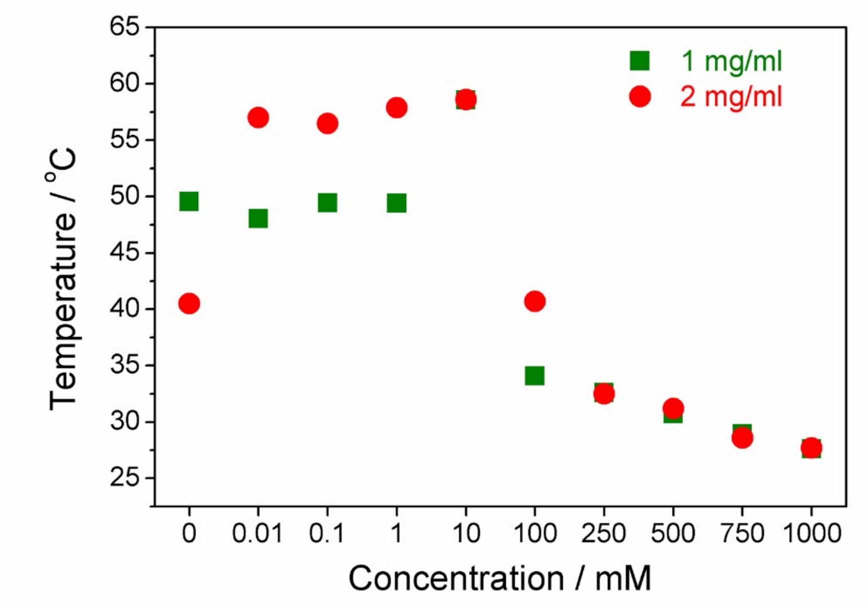

Figure S4. The effect of concentrations of poly(DEGEEA)-*r*-(Ribose) (1, 2 mg / mL) on the cloud points in the aqueous solution of NaBr (0-1000 mM).

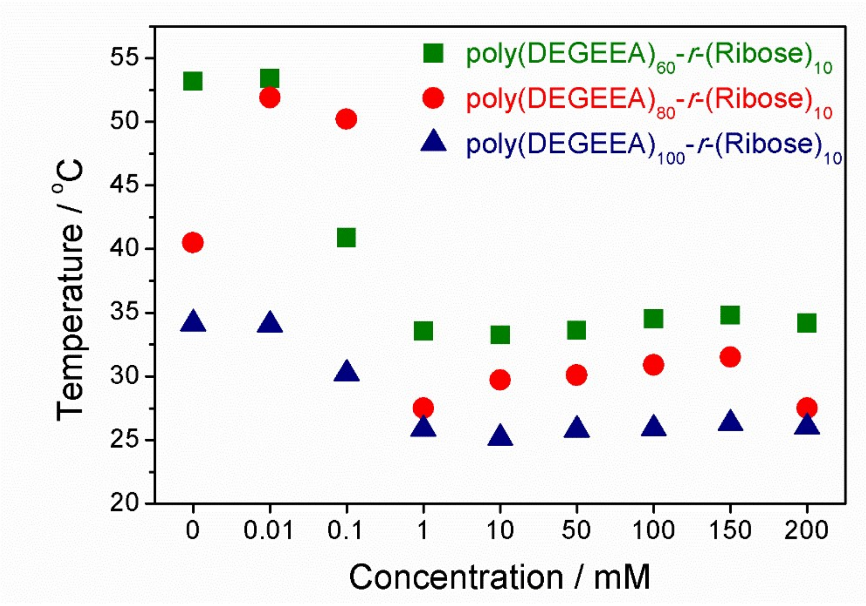

Figure S5. The effects of different contents of ribose on the cloud point of glycopolymers in the aqueous solution of $Cr(NO_3)_3$ (0-1000 mM). The concentrations of polymers in the solution are all 2 mg mL^{-1}.

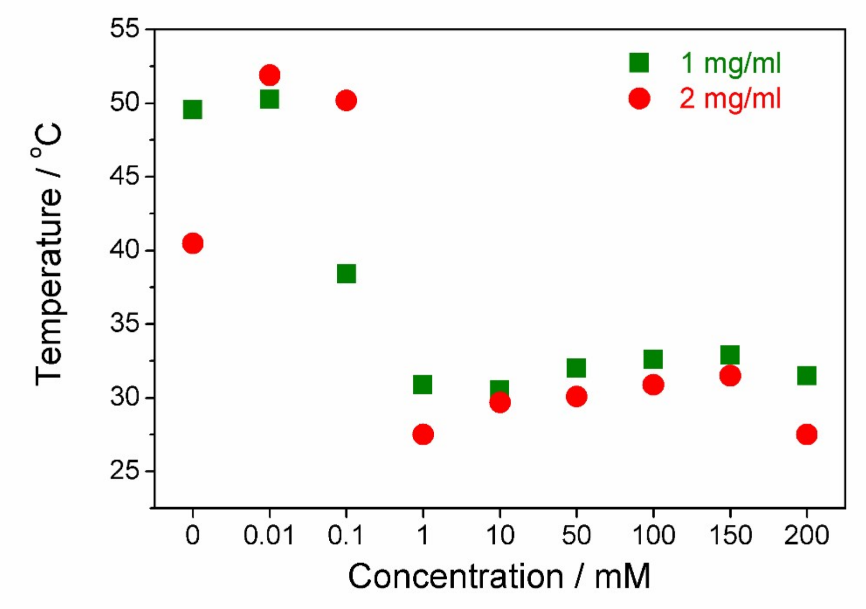

Figure S6. The effect of concentrations of poly(DEGEEA)-*r*-(Ribose) (1, 2 mg / mL) on the cloud points in the aqueous solution of $Cr(NO_3)_3$ (0-1000 mM).

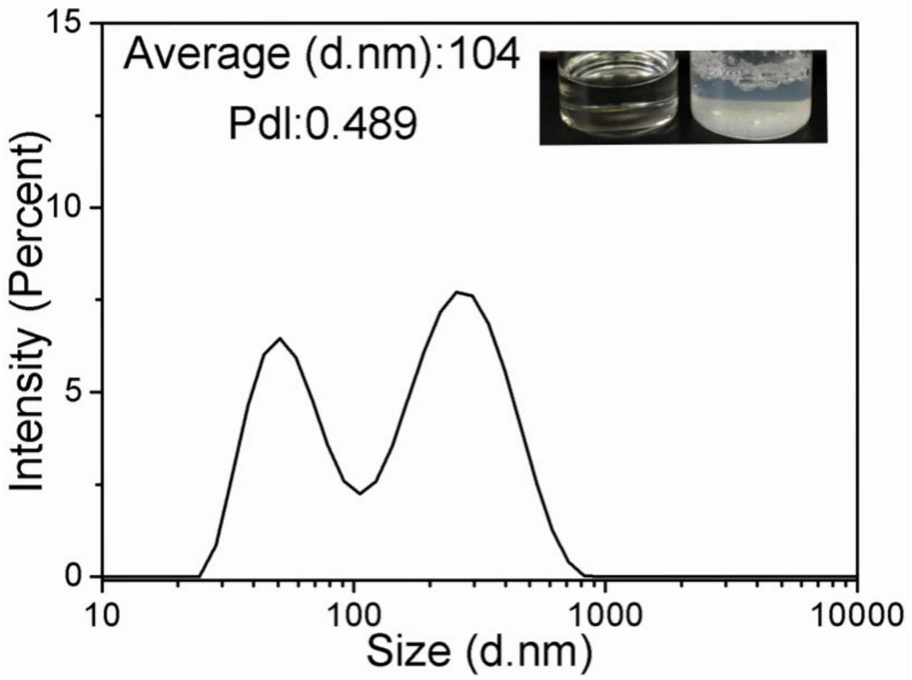

Figure S7. Size and size distribution of poly(Ribose) (2 mg mL^{-1}) in the aqueous solution of 1,4-phenylenebisboronic acid (0.2 mg mL^{-1}) by DLS. Inset: Images of poly(Ribose) (1 mL, 2 mg mL^{-1}) aqueous solution before (left) and after (right) the addition of 1,4-phenylenebisboronic acid (1 mL, 0.2 mg mL^{-1}).

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